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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/673,872	12/04/2000	Tony Wai-Chiu So	C7979U	5826

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EXAMINER	
WELTER, RACHAEL E	
ART UNIT	PAPER NUMBER
1611	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/673,872	WAI-CHIU SO ET AL.	
	Examiner	Art Unit	
	RACHAEL WELTER	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 May 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,8,12-16,19,21,23,24,26,29 and 139-163* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,8,12-16,19,21,23,24,26,29 and 139-163* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

5) ☐ Notice of Informal Patent Application

6) ☐ Other: _____.

DETAILED ACTION

Claim Status

Claims 1, 3-4, 8, 12-16, 19, 21, 23-24, 26, 29, and 139-163 are pending. Claims 2, 5-7, 9-11, 17-18, 20, 22, 25, 27-28, and 30-138 are cancelled.

Acknowledgements

Receipt of the amendment and remarks/arguments filed on 5/12/11 is acknowledged.

Withdrawn Rejections

The rejection of claims 1, 3-4, 8, 12-16, 19, 21, 23-24, 26, 29, and 139-163 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in light of applicant's amendments.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The rejection of claims 1, 3-4, 8, 12-16, 19, 26, 29, 139, 141, 143-144, and 162 rejected under 35 U.S.C. 103(a) as being unpatentable over JP 10-265343 (Machine Translation Attached Herein; Published: 1998) in view of Yu et al (EP0273202) is maintained.

JP '343 teaches topical preparations wherein monoxidil and dipropylene glycol are blended to restore hair (claim 1; paragraph 0005). Dipropylene glycol is 5-40 wt.% of the pharmaceutical preparation and other polyhydric alcohols chosen from 1,3-butylene glycol and propylene glycol can be added as well in an amount of 0.1-10 wt.% (claim 7). The preparation has a preferred pH of 5-8 (paragraph 0010). Minoxidil is present in the preparation in an amount of 0.1-10 wt.% (claim 2). The preparation also comprises 0.5-30 wt.% water and 50-90 wt.% lower alcohol (ethanol and isopropyl

alcohol) (paragraph 0014). The preparation can be used for external preparations, such as cream pharmaceuticals, ointments, aerosols, and lotions (paragraph 0015). Emulsifiers, higher alcohols (2-hexyl-1-decanol and isooctadecanol), perfumes, cooling agents, and color can also be blended into the preparations (paragraph 0013).

JP '343 does not teach the instant acid salt.

Yu et al teach additives such as hydroxy acids enhance the therapeutic effects of pharmaceutical and cosmetic actives in topical treatments. See page 2. The pharmaceutical or cosmetic active is utilized generally in the amount of 0.01-40% and the hydroxyl acid is used in the amount of 0.01-99%. See page 6. Yu teaches the use of 3% lactic acid with minoxidil to help the minoxidil dissolve in the solution and enhance penetration and the efficacy of minoxidil on hair growth. The pH of the solution is 4.7. See example 3.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Peck and Yu et al and utilize the instant acid. One would be motivated to do so since Yu teaches adding lactic acid dissolves minoxidil providing better penetration of minoxidil. Therefore, a skilled artisan would have been motivated to add an acid to form a minoxidil acid salt for enhanced penetration of minoxidil into the hair follicle.

Regarding the limitations directed to the amount of minoxidil, JP '343 teaches minoxidil in an amount of 0.1-10%. Thus, it would have been obvious to a skilled artisan at the time the invention was made to manipulate the concentration of minoxidil during routine optimization in order to achieve a concentration of at least 5% and more

specifically, 7.5 to 12% by weight. One would have been motivated to do so depending on the dosage strength and the needs of a particular patient population. Drug concentration is a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. *In re Antonie*, 559 F.2d 618, 195 USPQ 6 (CCPA 1977).

Regarding the instantly claimed ratio of ethanol to water, JP '343 sets forth a general range of components wherein the alcohol is utilized in an amount of 50-90 wt.% and water from 0.5-30 wt.%. Thus, it is within the skill of an artisan to look at the guidance provided by JP '343 and manipulate the concentrations (ratio) of water and ethanol depending on the concentration of the other components. It should be noted that generally difference in concentrations do not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such as concentration is critical. See *In re Aller,* 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Regarding the limitation, wherein "propylene glycol is present in an amount of less than 5%" and newly added claim 162, "wherein the composition is free of propylene glycol," it is noted that JP '343 teaches that 1,3-butylene glycol OR propylene glycol can be added to its preparation in an amount of 0.1-10 wt.%. Therefore, JP '343 envisages the absence of propylene glycol. Additionally, JP '343 suggests that the compound can be present at less than 5% since 0.1-10 wt.% encompasses the instant amount. According to MPEP 2144.05, "[A] prior art reference that discloses a range

encompassing a somewhat narrower claimed range is sufficient to establish a prima facie case of obviousness." *In re Peterson*, 315 F.3d 1325, 1330, 65 USPQ2d 1379, 1382-83 (Fed. Cir. 2003).

Regarding the limitation, "wherein the pharmaceutical composition upon actuation with a propellant forms a foam or mousse," it is noted that this limitation is intended use. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. In this case, since the combined prior art suggests all the components of the instant claims, the prior art structure is capable of performing a form or mousse with the addition of a propellant. If the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present as *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

The rejection of claims 21, 23-24, 146-151, 153-157, 159-160, and 163 rejected under 35 U.S.C. 103(a) as being unpatentable over JP 10-265343 (Machine Translation Attached Herein; Published: 1998) in view of Yu et al (EP0273202) and Chow et al (US Patent No. 4,515,810; Published 5/7/1985) is maintained.

JP '343 teaches topical preparations wherein monoxidil and dipropylene glycol are blended to restore hair (claim 1; paragraph 0005). Dipropylene glycol is 5-40 wt.% of the pharmaceutical preparation and other polyhydric alcohols chosen from 1,3-

butylene glycol and propylene glycol can be added as well in an amount of 0.1-10 wt.% (claim 7). The preparation has a preferred pH of 5-8 (paragraph 0010). Minoxidil is present in the preparation in an amount of 0.1-10 wt.% (claim 2). The preparation also comprises 0.5-30 wt.% water and 50-90 wt.% lower alcohol (ethanol and isopropyl alcohol) (paragraph 0014). The preparation can be used for external preparations, such as cream pharmaceuticals, ointments, aerosols, and lotions (paragraph 0015). Emulsifiers, higher alcohols (2-hexyl-1-decanol and isooctadecanol), perfumes, cooling agents, and color can also be blended into the preparations (paragraph 0013).

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Yu et al teach additives such as hydroxy acids enhance the therapeutic effects of pharmaceutical and cosmetic actives in topical treatments. See page 2. The pharmaceutical or cosmetic active is utilized generally in the amount of 0.01-40% and the hydroxyl acid is used in the amount of 0.01-99%. See page 6. Yu teaches the use of 3% lactic acid with minoxidil to help the minoxidil dissolve in the solution and enhance penetration and the efficacy of minoxidil on hair growth. The pH of the solution is 4.7. See example 3.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Peck and Yu et al and utilize the instant acid. One would be motivated to do so since Yu teaches adding lactic acid dissolves minoxidil providing better penetration of minoxidil. Therefore, a skilled artisan would have been motivated to add an acid to form a minoxidil acid salt for enhanced penetration of minoxidil into the hair follicle.

Additionally, JP '343 does not utilize a propellant to form a foam or mousse. JP '343 only teaches that its external preparations can be used as aerosols.

Chow et al teach quick-breaking foam formulations to deliver topical medicaments (abstract; column 3, lines 65-68--column 4, lines 1-2). Propellants utilized in its formulations include hydrocarbons, such as propane, isobutane or mixtures thereof (column 7, lines 63-64). Chow et al teach that foams have advantages over creams or ointments because they have a neater appearance and are easier to use than other topical preparations (column 5, lines 60-67). According to Chow et al, foams enable the medication to be administered quickly and the proper dose to be effectively controlled via a metered valve (column 5, lines 60—column 6, lines 1-2).

Therefore, it would have been obvious to an artisan of ordinary skill at the time the invention was made to utilize a propellant within the compositions of JP '343 to form a foam or mousse. One would have been motivated to do so since JP '343 discloses that its compositions can be formulated as aerosols and Chow et al teach that foams have a neater appearance and are easier to use than other topical preparations. Therefore, an ordinary skilled artisan would have been motivated to formulate the preparation into a foam for the obvious reason of increasing patient compliance.

Regarding the limitations directed to the amount of minoxidil, JP '343 teaches minoxidil in an amount of 0.1-10%. Thus, it would have been obvious to a skilled artisan at the time the invention was made to manipulate the concentration of minoxidil during routine optimization in order to achieve a concentration of at least 5% and more specifically, 7.5 to 12% by weight. One would have been motivated to do so depending

on the dosage strength and the needs of a particular patient population. Drug concentration is a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. *In re Antonie, 559 F.2d 618, 195 USPQ 6 (CCPA 1977).*

Regarding the instantly claimed ratio of ethanol to water, JP '343 sets forth a general range of components wherein the alcohol is utilized in an amount of 50-90 wt.% and water from 0.5-30 wt.%. Thus, it is within the skill of an artisan to look at the guidance provided by JP '343 and manipulate the concentrations (ratio) of water and ethanol depending on the concentration of the other components. It should be noted that generally difference in concentrations do not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such as concentration is critical. See *In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).*

Regarding the limitation, wherein "propylene glycol is present in an amount of less than 5%" and newly added claim 163, "wherein the composition is free of propylene glycol," it is noted that JP '343 teaches that 1,3-butylene glycol OR propylene glycol can be added in its preparation in an amount of 0.1-10 wt.%. Therefore, JP '343 suggests the absence of propylene glycol. Additionally, JP '343 suggests that the compound can be present at less than 5% since 0.1-10 wt.% encompasses the instant amount. According to MPEP 2144.05, "[A] prior art reference that discloses a range encompassing a somewhat narrower claimed range is sufficient to establish a prima

facie case of obviousness." *In re Peterson*, 315 F.3d 1325, 1330, 65 USPQ2d 1379, 1382-83 (Fed. Cir. 2003).

The rejection of claims 152 and 161 rejected under 35 U.S.C. 103(a) as being unpatentable over JP 10-265343 (Machine Translation Attached Herein; Published: 1998) in view of Yu et al (EP0273202) and Chow et al (US Patent No. 4,515,810; Published 5/7/1985) as applied to claims 21, 23-24, 146-151, 153-157, 159-160, and 163 above and in further view of Uchikawa et al (5,156,836) is maintained.

The rejection of claims 140 and 145 rejected under 35 U.S.C. 103(a) as being unpatentable over JP 10-265343 (Machine Translation Attached Herein; Published: 1998) in view of Yu et al (EP0273202) as applied to claims 1, 3-4, 8, 12-16, 19, 26, 29, 139, 141, 143-144, and 162 above and in further view of Uchikawa et al (5,156,836) is maintained.

The teachings of JP '343, Yu et al, and/or Chow et al have been set forth above.

JP '343, Yu et al, and/or Chow et al not teach the elected glycerol co-solvent or an antioxidant.

Uchikawa teaches a hair revitalizing composition that may comprise minoxidil. Uckikawa teaches conventional excipients used to formulate hair-revitalizing compositions include polyhydric alcohols such as glycerine and propylene glycol, antioxidants, etc. see column 4, lines 5-30.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings above and substitute the exemplified propylene glycol with the instantly claimed glycerol and arrive at the instant invention. One would have been motivated to do so since Uchikawa teaches both propylene glycol and glycerol are polyhydric alcohols conventionally used in the art. Therefore, an ordinary skilled artisan would have expected similar results using any conventional polyhydric alcohol in the composition of JP '343.

Further, it would have been obvious for a skilled artisan to further utilize a conventional excipient such as an antioxidant as taught by Uchikawa in the composition of JP '343. One would have been motivated to do so in order to prevent oxidation and degradation.

The rejection of claim 158 rejected under 35 U.S.C. 103(a) as being unpatentable over JP 10-265343 (Machine Translation Attached Herein; Published: 1998) in view of Yu et al (EP0273202) and Chow et al (US Patent No. 4,515,810; Published 5/7/1985) as applied to claims 21, 23-24, 146-151, 153-157, 159-160, and 163 above and in further view of Peck et al (WO 88/01863) is maintained.

The rejection of claim 142 rejected under 35 U.S.C. 103(a) as being unpatentable over JP 10-265343 (Machine Translation Attached Herein; Published: 1998) in view of Yu et al (EP0273202) as applied to claims 1, 3-4, 8, 12-

16, 19, 26, 29, 139, 141, 143-144, and 162 above and in further view of Peck et al (WO 88/01863) is maintained.

The teachings of JP '343, Yu et al, and/or Chow et al have been set forth above.

JP '343, Yu et al, and/or Chow et al do not utilize Polysorbate 60.

Peck teaches a quick breaking foam to treat baldness comprising 1-5% minoxidil and various surfactants including Tween 80 (polysorbate) and Span 60 to improve the stability of the composition (pg. 6, lines 20-25).

Therefore, it would have been obvious to an artisan of ordinary skill at the time the invention was made to utilize Polysorbate 60 in the preparation of JP '343. One would have been motivated to do so since JP '343 teaches preparations comprising minoxidil and Peck suggests it as a stabilizer in minoxidil quick-breaking foams. Thus, an artisan would have a reasonable expectation of success that the instant emulsifier would modify the surface tension and improve the physical stability of JP '343's minoxidil formulation.

Response to Arguments

Applicant's arguments filed 5/12/11 have been fully considered but they are not persuasive.

Applicant argues that primary reference, JP 10-265343 does not constitute prior art against the instant application. The instant application has an effective priority date of April 22, 1998 claiming foreign priority to Australian Patent Application No. PP3107. Applicant argues that the effective date of JP 10-265343 is the date the reference was

published, October 6, 1998, which is clearly after the earliest claimed priority date of the present application.

However, the examiner respectfully disagrees with applicant that JP '343 is not prior art. The examiner acknowledges that applicant is claiming priority to the Australia Patent Application. However, the examiner fails to find sufficient support for the instant independent claims in the Australia Application. "To comply with the written description requirement of 35 U.S.C. 112, para. 1, or to be entitled to an earlier priority date or filing date under 35 U.S.C. 119, 120, or 365(c),each claim limitation must be expressly, implicitly, or inherently supported in the originally filed disclosure." See MPEP 2163.05. Independent claims 1 and 21 are drawn optionally to one or more excipients selected from a higher alcohol, a vitamin, a preservative, etc. However, the Australia Application does not disclose the generic excipients or even exemplify specific excipients that would fall under the categories of the recited excipients in its examples. For example there is no specific refrigerant, UV absorber, dye, or gelling agent exemplified in the Australian Application. See *In re Gosteli*, 872 F.2d 1008, 10 USPQ2d 1614 (Fed. Cir. 1989) (generic and subgeneric claims in the U.S. application were not entitled to the benefit of foreign priority where the foreign application disclosed only two of the species encompassed by the broad generic claim and the subgeneric Markush claim that encompassed 21 compounds). Furthermore, the instant claims recite a broader ratio of water to lower alcohol (9:1 to 1:9 by volume) than the Australia Application which teaches 1:1 to 1:3 and more preferably 1:1.7 to 1:1.9 (see pg. 2, lines 16-17).

As such, claims 1 and 21 and their dependent claims (claims 3-4, 8, 12-16, 19, 23-24, 26, 29, and 139-163) will not be entitled to the benefit of the priority date of April 22, 1998. The earliest priority date of the application will be April 20, 1999, which was when the 371 of PCT/AU99/00294 was filed. Applicant should note that this date is after JP '343's publication date of October 6, 1998.

As such, it is the examiner's position that the rejections should be maintained for the reasons stated above.

New Rejections

The following rejections constitute new grounds for rejection necessitated by amendment.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3-4, 8, 12-16, 19, 21, 23-24, 26, 29, and 139-163 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 21 recite "...minoxidil lactate, as sole hair-growing active present in the composition…" and then further recite that optionally one or more excipients can be present including "a hair generating agent." Therefore, the metes and bounds of the claim are unclear and it cannot be determined if applicant intended minoxidil to be the

only hair growing active in the composition or if multiple hair growing actives can be present. Applicant's clarification is respectfully requested.

Claims 3-4, 8, 12-16, 19, 23-24, 26, 29, and 139-163 are rejected as being dependent on rejected base claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-4, 8, 12-16, 19, 26, 29, 139, 143-144, and 162 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/03638 to Navarro et al in view of WO 97/12602 to Weiner et al and Yu et al (EP0273202).

Navarro teaches a minoxidil-based composition for promoting hair growth. The solvent system comprises the combination of ethanol or isopropyl alcohol and propylene glycol or polyethylene glycol to solubilize minoxidil but Navarro teaches that a significant amount of propylene glycol makes the hair greasy and shiny (pg. 2 of translation). Navarro teaches using cyclodextrin to reduce the amount of solvent required to solubilize minoxidil (pg. 3 of translation). Navarro's hair care composition contains 0.1-7% minoxidil, 0.1-5% cyclodextrin, 0.5-15% minoxidil solvent (propylene glycol), 30-50% monoalcohol (ethanol or isopropanol), and water (abstract; examples). Navarro also teaches that solvents can be utilized other than propylene glycol including N-methylpyrrolidone or diethylene glycol monoethyl ethers (pg. 3 of translation).

Navarro does not teach the use of lactic or acetic acid.

Weiner teaches a topical composition for minoxidil. WO discloses that making materials more hydrophilic, improves penetration through the hair follicle. Weiner teaches that a number of different modifications may be made to the minoxidil. One such modification is provided by reacting minoxidil with an organic acid such as lactic acid. The minoxidil may also be converted to a salt by reacting it with a cyclodextrin (pg. 3). Weiner states that the use of a minoxidil acid salt addition provides substantial

penetration and cyclodextrin salt addition is the “next best” (pg. 7). Weiner teaches encapsulation of minoxidil increases penetration of the active across the skin.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Navarro et al and Weiner et al and substitute Navarro’s cyclodextrin with the instant acid to convert minoxidil into a salt. One would be motivated to do so since Weiner teaches that by converting minoxidil to a hydrophilic compound, it penetrates the skin penetrate. More specifically, Weiner teaches the conversion of minoxidil into a salt form by reacting it with an organic acid such as instant lactic acid or with cyclodextrin and notes that although both provide penetration of minoxidil, the acid salt addition has a better effect than the cyclodextrin salt addition. Therefore, one would have been motivated to use an acid salt addition to convert minoxidil into a hydrophilic compound rather than Navarro’s cyclodextrin since Weiner teaches the acid salt addition has better penetration into the skin.

With regard to the pH, it is the examiner’s position that the combination of Navarro and Weiner would render a pH in the acidic range because of the lactic acid. The examiner cites Yu et al (EP ‘202) to support this position wherein lactic acid and minoxidil yield a composition with a range of 4.6, which is very close to the instant range of 5.0 to 7.0. According to MPEP 2144.05, "A prima facie case of obviousness exists where the claimed ranges and prior art ranges do not overlap but are close enough that one skilled in the art would have expected them to have the same properties." *Titanium Metals Corp. of America v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985).

With regard to the instantly claimed ratio, Navarro sets forth a general range of components wherein a monoalcohol is utilized in an amount of 30-50% and water to balance, thus it is within the skill of an artisan to look at the guidance provided by Navarro and manipulate the concentrations (ratio) of water and ethanol depending on the concentration of the other components. It should be noted that generally difference in concentrations do not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such as concentration is critical. See In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

With regard to claim 4, 7.5% is considered obvious over Navarro's teaching that the minoxidil may be in the amount of 7%. It would have been obvious to a skilled artisan at the time the invention was made to manipulate the concentration of minoxidil during routine optimization in order to achieve a concentration of 7.5 to 12% by weight. One would have been motivated to do so depending on the desired "strength" of the composition and to meet the needs of a particular patient population. Drug concentration is a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. *In re Antonie,* 559 F.2d 618, 195 USPQ 6 (CCPA 1977).

Regarding the limitation, "wherein the pharmaceutical composition upon actuation with a propellant forms a foam or mousse," it is noted that this limitation is intended use. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to

patentably distinguish the claimed invention from the prior art. In this case, since the combined prior art suggest all the components of the instant claims, the prior art structure is capable of performing a form or mousse with the addition of a propellant. If the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present as *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Regarding the limitation of claim 162, wherein the composition is free of propylene glycol, it is noted that Navarro also teaches that other solvents can be utilized other than propylene glycol including N-methylpyrrolidone or diethylene glycol monoethyl ethers (pg. 3 of translation). Therefore, it is the examiner's position that Narvarro envisages compositions without propylene glycol.

Furthermore, assuming that applicant will argue that the instant claims exclude components other than those expressly recited (i.e. the inclusion of Weiner's lipid vesicle), it is the examiner's position that the recited optional excipients including "thickener," and "gelling agent" could read on the prior art's lipid vesicles. Since applicant has not defined these excipients any further to encompass particular species, the examiner maintains the position that the instant claims do not exclude Weiner's lipid vesicle.

Claims 21, 23-24, 146-151, 153-156, 159-160, and 163 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/03638 to Navarro et al in view of

WO 97/12602 to Weiner et al, Yu et al (EP0273202), and Chow et al (US Patent No. 4,515,810; Published 5/7/1985).

Navarro teaches a minoxidil-based composition for promoting hair growth. The solvent system comprises the combination of ethanol or isopropyl alcohol and propylene glycol or polyethylene glycol to solubilize minoxidil but Navarro teaches that a significant amount of propylene glycol makes the hair greasy and shiny (pg. 2 of translation). Navarro teaches using cyclodextrin to reduce the amount of solvent required to solubilize minoxidil (pg. 3 of translation). Navarro's hair care composition contains 0.1-7% minoxidil, 0.1-5% cyclodextrin, 0.5-15% minoxidil solvent (propylene glycol), 30-50% monoalcohol (ethanol or isopropanol), and water (abstract; examples). Navarro also teaches that solvents can be utilized other than propylene glycol including N-methylpyrrolidone or diethylene glycol monoethyl ethers (pg. 3 of translation).

Navarro does not teach the use of lactic or acetic acid.

Weiner teaches a topical composition for minoxidil. WO discloses that making materials more hydrophilic, improves penetration through the hair follicle. Weiner teaches that a number of different modifications may be made to the minoxidil. One such modification is provided by reacting minoxidil with an organic acid such as lactic acid. The minoxidil may also be converted to a salt by reacting it with a cyclodextrin (pg. 3). Weiner states that the use of a minoxidil acid salt addition provides substantial penetration and cyclodextrin salt addition is the "next best" (pg. 7). Weiner teaches encapsulation of minoxidil increases penetration of the active across the skin.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Navarro et al and Weiner et al and substitute Navarro's cyclodextrin with the instant acid to convert minoxidil into a salt. One would be motivated to do so since Weiner teaches that by converting minoxidil to a hydrophilic compound, it penetrates the skin penetrate. More specifically, Weiner teaches the conversion of minoxidil into a salt form by reacting it with an organic acid such as instant lactic acid or with cyclodextrin and notes that although both provide penetration of minoxidil, the acid salt addition has a better effect than the cyclodextrin salt addition. Therefore, one would have been motivated to use an acid salt addition to convert minoxidil into a hydrophilic compound rather than Navarro's cyclodextrin since Weiner teaches the acid salt addition has better penetration into the skin.

With regard to the pH, it is the examiner's position that the combination of Navarro and Weiner would render a pH in the acidic range because of the lactic acid. The examiner cites Yu et al (EP '202) to support this position wherein lactic acid and minoxidil yield a composition with a range of 4.6, which is very close to the instant range of 5.0 to 7.0. According to MPEP 2144.05, "A prima facie case of obviousness exists where the claimed ranges and prior art ranges do not overlap but are close enough that one skilled in the art would have expected them to have the same properties." *Titanium Metals Corp. of America v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985).

Additionally, Navarro does not utilize a propellant in its compositions to form a foam or mousse.

Chow et al teach quick-breaking foam formulations to deliver topical medicaments (abstract; column 3, lines 65-68--column 4, lines 1-2). Propellants utilized in its formulations include hydrocarbons, such as propane, isobutane or mixtures thereof (column 7, lines 63-64). Chow et al teach that foams have advantages over creams or ointments because they have a neater appearance and are easier to use than other topical preparations (column 5, lines 60-67). According to Chow et al, foams enable the medication to be administered quickly and the proper dose to be effectively controlled via a metered valve (column 5, lines 60—column 6, lines 1-2).

Therefore, it would have been obvious to an artisan of ordinary skill at the time the invention was made to utilize a propellant within the compositions of Navarro to form a foam or mousse. One would have been motivated to do so since Navarro discloses that its compositions can be formulated as aerosols and Chow et al teach that foams have a neater appearance and are easier to use than other topical preparations. Therefore, an ordinary skilled artisan would have been motivated to formulate the preparation into a foam for the obvious reason of increasing patient compliance.

With regard to the instantly claimed ratio of lower alcohol and water, Navarro sets forth a general range of components wherein a monoalcohol is utilized in an amount of 30-50% and water to balance, thus it is within the skill of an artisan to look at the guidance provided by Navarro and manipulate the concentrations (ratio) of water and ethanol depending on the concentration of the other components. It should be noted that generally difference in concentrations do not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such as

concentration is critical. See In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

With regard to claim 146, 7.5% is considered obvious over Navarro's teaching that the minoxidil may be in the amount of 7%. It would have been obvious to a skilled artisan at the time the invention was made to manipulate the concentration of minoxidil during routine optimization in order to achieve a concentration of 7.5 to 12% by weight. One would have been motivated to do so depending on the desired "strength" of the composition and to meet the needs of a particular patient population. Drug concentration is a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. *In re Antonie,* 559 F.2d 618, 195 USPQ 6 (CCPA 1977).

Regarding the limitation of claim 163, wherein the composition is free of propylene glycol, it is noted that Navarro also teaches that other solvents can be utilized other than propylene glycol including N-methylpyrrolidone or diethylene glycol monoethyl ethers (pg. 3 of translation). Therefore, it is the examiner's position that Narvarro envisages compositions without propylene glycol.

Furthermore, assuming that applicant will argue that the instant claims exclude components other than those expressly recited (i.e. the inclusion of Weiner's lipid vesicle), it is the examiner's position that the recited optional excipients including "thickener," and "gelling agent" could read on the prior art's lipid vesicles. Since applicant has not defined these excipients any further to encompass particular species,

the examiner maintains the position that the instant claims do not exclude Weiner's lipid vesicle

Claims 140 and 145 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/03638 to Navarro et al in view of WO 97/12602 to Weiner et al and Yu et al (EP0273202) as applied to claims 1, 3-4, 8, 12-16, 19, 26, 29, 139, 143- 144, and 162 above and in further view of Uchikawa et al (5,156,836)

Claims 152 and 161 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/03638 to Navarro et al in view of WO 97/12602 to Weiner et al, Yu et al (EP0273202), and Chow et al (US Patent No. 4,515,810; Published 5/7/1985) as applied to claims 21, 23-24, 146-151, 153-156, 159-160, and 163 above and in further view of Uchikawa et al (5,156,836).

The teachings of Navarro, Weiner, Yu, and/or Chow et al have been set forth above.

Navarro, Weiner, Yu, and/or Chow et al do not teach the elected glycerol co-solvent or an antioxidant.

Uchikawa teaches a hair revitalizing composition that may comprise minoxidil. Uckikawa teaches conventional excipients used to formulate hair-revitalizing compositions include polyhydric alcohols such as glycerine and propylene glycol, antioxidants, etc. see column 4, lines 5-30.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings above and substitute the

exemplified propylene glycol with the instantly claimed glycerol and arrive at the instant invention. One would have been motivated to do so since Uchikawa teaches both propylene glycol and glycerol are polyhydric alcohols conventionally used in the art. Therefore, an ordinary skilled artisan would have expected similar results using any conventional polyhydric alcohol in the composition of Navarro.

Further, it would have been obvious for a skilled artisan to further utilize a conventional excipient such as an antioxidant as taught by Uchikawa in the composition of Navarro. One would have been motivated to do so in order to prevent oxidation and degradation.

Claim 142 is rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/03638 to Navarro et al in view of WO 97/12602 to Weiner et al and Yu et al (EP0273202) as applied to claims 1, 3-4, 8, 12-16, 19, 26, 29, 139, 143- 144, and 162 above and in further view of Peck et al (WO 88/01863).

Claim 158 is rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/03638 to Navarro et al in view of WO 97/12602 to Weiner et al, Yu et al (EP0273202), and Chow et al (US Patent No. 4,515,810; Published 5/7/1985) as applied to claims 21, 23-24, 146-151, 153-156, 159-160, and 163 above and in further view of Peck et al (WO 88/01863).

The teachings of Navarro, Weiner, Yu, and/or Chow et al have been set forth above.

Navarro, Weiner, Yu, and/or Chow et al do not utilize Polysorbate 60.

Peck teaches a quick breaking foam to treat baldness comprising 1-5% minoxidil and various surfactants including Tween 80 (polysorbate) and Span 60 to improve the stability of the composition (pg. 6, lines 20-25).

Therefore, it would have been obvious to an artisan of ordinary skill at the time the invention was made to utilize Polysorbate 60 in the preparation of Navarro. One would have been motivated to do so since Navarro teaches preparations comprising minoxidil and Peck suggests it as a stabilizer in formulations comprising minoxidil. Thus, an artisan would have a reasonable expectation of success that the instant emulsifier would modify the surface tension and improve the physical stability of Navarro's minoxidil formulation.

Claim 141 is rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/03638 to Navarro et al in view of WO 97/12602 to Weiner et al and Yu et al (EP0273202) as applied to claims 1, 3-4, 8, 12-16, 19, 26, 29, 139, 143- 144, and 162 above and in further view of Gibson (US Patent No. 4,871,839).

Claim 157 is rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/03638 to Navarro et al in view of WO 97/12602 to Weiner et al, Yu et al (EP0273202), and Chow et al (US Patent No. 4,515,810; Published 5/7/1985) as applied to claims 21, 23-24, 146-151, 153-156, 159-160, and 163 above and in further view of Gibson (US Patent No. 4,871,839).

The teachings of Navarro, Weiner, Yu, and/or Chow et al have been set forth above.

Navarro, Weiner, Yu, and/or Chow et al do not teach cetyl alcohol or stearyl alcohol in its compositions.

Gibson teaches cosmetic and pharmaceutical compositions for topical application to human skin, containing a derivative of minoxidil which is particularly useful in promoting or enhancing the growth of hair, especially on the human scalp (column 1, lines 5-10) The compositions can comprise emollients including cetyl and stearyl alcohol (column 6, lines 62-65; examples 9-12).

Therefore, it would have been obvious to an artisan of ordinary skill at the time the invention was made to include cetyl and/or stearyl alcohol in the minoxidil formulations of Navarro. One would have been motivated to do so since Gibson teaches that cetyl and stearyl alcohol are conventional emollients utilized in topical formulations comprising minoxidil. Thus, if an ordinary skilled artisan desired to soothe and soften the skin/scalp, one would be motivated to add cetyl and/or stearyl alcohol to its topical formulations.

Conclusion

Claims 1, 3-4, 8, 12-16, 19, 21, 23-24, 26, 29, and 139-163 are rejected. No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to RACHAEL E. WELTER whose telephone number is (571) 270-5237. The examiner can normally be reached 7:30-5:00 Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached at 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

REW

/Lakshmi S Channavajjala/

Primary Examiner, Art Unit 1611